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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/687,996	10/17/2003	Lothar Steidler	2676-6096US	1934

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EXAMINER	
SLOBODYANSKY, ELIZABETH	
ART UNIT	PAPER NUMBER
1652	
MAIL DATE	DELIVERY MODE
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/687,996	STEIDLER, LOTHAR	
	Examiner	Art Unit	
	Elizabeth Slobodyansky, PhD	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *30 April 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-63* is/are pending in the application.

4a) Of the above claim(s) *11 and 18-20* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-10,12-17 and 21-63* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on April 30, 2007 has been entered.

The amendment filed April 30, 2007 amending claims 1-10, 12, 13, 21-30 and adding claims 31-63 has been entered.

Claims 1-63 are pending. Claims 11 and 18-20 have been previously withdrawn.

Claim Objections

Claim 5 is objected to because it appears that "further" is missing between "is" and "transformed" (lines 3-4).

Claim 12 is objected to because "a" is not needed before "*Lactococcus* species of claim 5".

Claim 62 is objected to because a period is missing at the end of the claim.

Appropriate correction is required.

Applicant is advised that should claim 22 be found allowable, claim 62 will be objected to under 37 CFR 1.75 as being a substantial duplicate thereof. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k). Both claims are drawn to a defect in SEQ ID NOs: 3 or 5.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 21, 23-30, 43-61 and 63 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claim 21, with dependent claims 24-26 and 30, claim 43, with dependent claims 44, 46-52, 60, 61, are drawn to an isolated *Lactococcus* bacterium comprising a defective thymidylate synthase gene. Claim 63 is drawn to *Lactococcus* bacterium comprising a defective thymidylate synthase Claims 23 and 27-29 dependent from claim 21 and claims 45 and 53-59 dependent from claim 43, limit the *Lactococcus*

bacterium to *Lactococcus lactis*. Therefore, the claims recite the genus of *Lactococcus* bacterium comprising a defective thymidylate synthase gene, said *Lactococcus* bacterium comprising both naturally occurring defects in thymidylate synthase gene and defects caused by molecular biological techniques, said defects resulting in encoding an active and inactive thymidylate synthase. Furthermore, the genus of *Lactococcus* species is diverse genus that encompassing thymidylate synthase gene or genes from any species of *Lactococcus*, including the subgenus of thymidylate synthase gene(s) from any subspecies of *L. lactis*.

The Court of Appeals for the Federal Circuit has recently held that a "written description of an invention involving a chemical genus, like a description of a chemical species, 'requires a precise definition, such as be structure, formula [or] chemical name,' of the claimed subject matter sufficient to distinguish it from other materials." University of California v. Eli Lilly and Co., 1997 U.S. App. LEXIS 18221, at *23, quoting Fiers v. Revel, 25 USPQ2d 1601, 1606 (Fed. Cir. 1993) (bracketed material in original). To fully describe a genus of genetic material, which is a chemical compound, applicants must (1) fully describe at least one species of the claimed genus sufficient to represent said genus whereby a skilled artisan, in view of the prior art, could predict the structure of other species encompassed by the claimed genus and (2) identify the common characteristics of the claimed molecules, e.g., structure, physical and/or chemical characteristics, functional characteristics when coupled with a known or disclosed correlation between function and structure, or a combination of these.

In the instant specification the genus of the genes of *Lactococcus* thymidylate synthase gene(s), including the subgenus of *L. lactis* thymidylate synthase gene(s), is represented by a single thymidylate synthase from *L. lactis* subsp. *lactis* that is disrupted by a functional human interleukin-10 expression cassette. The art teaches that *L. lactis* has other thyA genes that are not homologous to SEQ ID NOs: 3 or 5 (Ross et al., below). The specification fails to describe any other representative species *Lactococcus* thymidylate synthase gene(s) by any identifying characteristics or properties other than the functionality of being *Lactococcus* thymidylate synthase gene(s).

The specification fails to define those structural features of *Lactococcus* thymidylate synthase gene(s) that are commonly possessed by members of the genus that distinguish them from others. The specification fails to provide the structure and function correlation common to all members of the genus of *Lactococcus* thymidylate synthase gene(s). Thus, one skilled in the art cannot visualize or recognize the identity of the members of the genus.

Given this lack of description of representative species encompassed by the genus of the claims, the specification fails to sufficiently describe the claimed invention in such full, clear, concise, and exact terms that a skilled artisan would recognize that applicants were in possession of the claimed invention at the time of filing.

Claims 21, 23-30, 43-61 and 63 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a *Lactococcus* bacterium

comprising a disrupted thymidylate synthase gene, said gene comprising SEQ ID NOs: 1 and 2, including comprising SEQ ID NOs: 3 or 5, does not reasonably provide enablement for a *Lactococcus* bacterium comprising a disrupted thymidylate synthase gene having 5' and 3' regions with less than 90% identity to SEQ ID NOs: 1 and 2 or an undefined percent identity to SEQ ID NOs: 3 or 5. It does not provide enablement for a defect in TS gene other than resulting in encoding an inactive thymidylate synthase. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, how to make and/or use the invention commensurate in scope with these claims.

Factors to be considered in determining whether undue experimentation is required, are summarized in In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988). They include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims.

The specification does not support the broad scope of the claim which encompasses comprising a disrupted thymidylate synthase gene from any *Lactococcus* bacterium having no known identity to SEQ ID NOs: 1 and 2 or SEQ ID NOs:3 or 5. The specification does not teach thymidylate synthase genes from other species of *Lactococcus* including other *subspecies of L. lactis*. While recombinant hybridization techniques are known, only highly homologous sequences can be identified using a

given nucleic acid sequence. The state of the art provides no reasonable expectation of success in obtaining nucleic acid encoding a thymidylate synthase gene that is flanked by sequences other than SEQ ID NOs: 1 and 2 and having an unknown identity to SEQ ID NOs: 3 or 5 and the result of such screening is unpredictable.

Without sufficient guidance, beyond that provided, disruption of thymidylate synthase genes of an unknown structure is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. The scope of the claims must bear a reasonable correlation with the scope of enablement (In re Fisher, 166 USPQ 19 24 (CCPA 1970)).

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-10, 12-17 and 21-63 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1-10, 12-17 and 21-63 are unclear as reciting "a defective thymidylate synthase gene" or "a defect" in said gene. It is impossible to know the metes and bounds of the claims without knowing what kind of defect is introduced. The defect can result in a gene encoding either an active or inactive thymidylate synthase.

Claim 5 recites "functional thymidylate synthase gene". The metes and bounds of the term are unclear as a gene may have different functions in addition to encoding a functional thymidylate synthase.

Claim 21 is further unclear because it recites a bacterium comprising a genome. Every bacterium comprises a genome. It further recites "a means for encoding a defective thymidylate synthase gene". The metes and bounds of "a means" are not defined in the specification and are not clear.

Claim 22 is confusing as reciting "strain of *Lactococcus* bacterium comprises a thymidylate synthase gene selected from the group consisting of SEQ ID NO:3 and SEQ ID NO:5". The specification teaches that SEQ ID NO:5 is a mutant version of SEQ ID NO:3 (page 11, [0036]). Similarly, claims 31, 33.

Claims 62 and 63 are confusing because it is unclear how "an improvement" limits "a defect". Furthermore, SEQ ID NO: 5 already has a defect compared with SEQ ID NO:3. Claim 63 is further unclear because the relationship between SEQ ID NOs: 3 or 5 and thymidylate synthase is unclear. The bacterium may comprise a defective thymidylate synthase that is added thereto not necessarily due to disruption of SEQ ID NOs: 3 or 5, for example.

Claims not specifically discussed herein are rejected as dependent from the rejected base claim.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-10, 12-17, 21, 23-30, 32 and 34-61 are rejected under 35 U.S.C. 102(b) as being anticipated by Ross et al.

Ross et al. (App. Environ. Microbiology (1990), Vol. 56, pages 2156-2163) teach a *Lactococcus lactis* subsp. *lactis* comprising *thyA* gene (page 2157, 2nd column). It was shown be chromosomally (not plasmid) encoded (paragraph bridging pages 2158-2159). Said gene comprises at least 100 contiguous nucleotides that are at least 90% identical to a region of SEQ ID NOs: 1 and 2. Said gene is construed as a mutant of SEQ ID NOs: 3 or 5.

Response to Arguments

Applicant's arguments filed April 30, 2007 have been fully considered but they are not persuasive.

Applicant argues the 112, 6th paragraph rejection (Remarks, pages 12-13). However, said rejection was not made.

With regard to the 112, 1st paragraph written description rejection, Applicant argues that 3 strains of *L. lactis* thymidylate synthase genes have up to 89% identity (page 14). This is not persuasive because the currently rejected claims are not limited to

said strains. It is known that there are other lactococcal *thyA* genes that are not sufficiently homologous to SEQ ID NOs: 3 or 5 (Ross, *supra*, page 2160, 1st column). With regard to the 112, 1st paragraph enablement rejection, Applicant argues that "a skilled person will be able to introduce a defect into the thymidylate synthase gene of any member of the *Lactococcus* species" (page 16). This is not persuasive because while the techniques to introduce the defect are available, without knowing the sequence they are not applicable.

With regard to the 112, 2nd paragraph rejection, the outstanding rejections not reiterated above are withdrawn in view of the amendment and Applicant's arguments. The rejection of the new claims is explained above.

The 103(a) rejection is withdrawn in view of the amendment and Applicant's arguments (pages 19-20).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Elizabeth Slobodyansky, PhD whose telephone number is 571-272-0941. The examiner can normally be reached on M-F 10:00 - 6:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapura Achutamurthy, PhD can be reached on 571-272-0928. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Elizabeth Slobodyansky, PhD
Primary Examiner
Art Unit 1652

January 18, 2007

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

E. Slobodyansky

Elizabeth Slobodyansky, PhD
Primary Examiner
Art Unit 1652

July 23, 2007